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COMPLETE SPECIFICATION

Medicated Lozenges

We, MERCK & CO., INC., a corporation duly organised and existing under the laws of the State of New Jersey, United States of America, of Rahway, New Jersey, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to medicated candy lozenges.

The preparation of candy lozenges is a difficult and critical art. Successful preparation requires heating a mixture of sugar i.e. sucrose, and glucose in water until a clear supersaturated solution is formed, thorough mixing of the solution and subsequent uniform deposition of solids by means of controlled cooling rates. The addition of solid (e.g. therapeutic) materials to the molten candy mass radically alters the structure of the candy probably by modifying its density or hardness, often resulting in a product which is excessively soft and tacky and therefore unuseable. The addition of solid materials may also cause inversion of the sugar in solution, thereby preventing the formation of a hard candy matrix.

For these and other reasons, it has hitherto been necessary in the preparation of medicated candy lozenges to limit the medicament to a small and often insufficient amount.

In accordance with this invention a process has been found which makes it possible to incorporate as much as from 8—10% by weight of a medicament, based on the weight of the candy base, into a candy lozenge without appreciably altering the hard candy structure necessary for the proper formation of the lozenge. This process comprises preparing a molten candy base consisting essentially of sucrose and glucose, separately heating a mixture of the powdered medicament and a polyethylene glycol having an average molecular weight in the range 4,000 — 20,000 until a uniform dispersion or solution of the medicament in the polyethylene glycol is obtained, blending the said dispersion or solution with the molten candy base in an amount of from 2—16% by weight, based on the candy base, and forming the blend into lozenges. The characteristic feature of this process is the presence of a small quantity of polyethylene glycol which surprisingly makes it possible to solubilise substantially larger quantities of medicament in the molten candy base. Subsequently, when the product is concentrated and cooled the medicament co-solidifies with the sucrose and glucose thus becoming uniformly dispersed in the hard candy matrix, producing an excellent lozenge which is free of opaque spots and also free of grittiness.

The polyethylene glycols which are utilised in accordance with this invention are polymers of ethylene oxide having the general formula $HOCH_2(CH_2OCH_2)_nCH_2OH$, where n represents the average number of oxyethylene groups. The specific "n" value to be used depends on the characteristics sought in the final product. As the average molecular weight of the polyethylene glycol increases, the hygroscopicity and the solvent power decrease and the viscosity of its aqueous solutions increases as does its melting point. Of particular utility in this invention is a polyethylene glycol, known as polyethylene glycol 6,000, which is a low melting point polyethylene glycol having a m.p. of 60—63° C.

When the medicament is added to the glycol and the mixture heated, the polyethylene glycol melts and a uniform dispersion or solution of the medicament in the molten glycol is formed. The exact temperature at which this occurs will depend on the glycol and the medicament, but usually it will be around 90° C. The uniform dispersion or solution is then blended with the molten candy base, usually at a temperature in the range 90—100° C. The blend is then formed into lozenges by conventional means. This ability to form the candy lozenge at a relatively low temperature

[illegible]

makes it possible to use medicaments which would decompose at the higher temperatures that previously were necessary for the formation of a candy lozenge without the use of polyethylene glycol.

The term "glucose" as used herein is intended to include substances containing gluclose, such as, for example, corn syrup.

As mentioned, the candy base consists essentially of sucrose and glucose. By this is meant that sucrose and glucose are the principal ingredients of the base, but that there may also be present minor amounts of other materials, particularly flavouring agents and dyes, as may be common in the art, and being such that the hard candy matrix is not destroyed. Preferably the candy base comprises from 60—85% by weight sucrose and from 15—40% by weight of glucose. While the quantities of polyethylene glycol and medicament may vary, the glycol should preferably amount to about 1—6% and the medicament about 1—10% by weight. Where citric acid is added, the quantity is about 1 to 3 parts by weight of the candy base.

The following examples are not intended to limit the scope of applicants' invention but are considered illustrative of typical lozenge preparations according to this invention.

EXAMPLE 1

Candy base:	
Sucrose	35.0 kg.
Corn syrup 43° Baume	21.0 kg.
Medicament mixture:	
Polyethylene glycol (6,000 m.w.)	2.75 kg.
Acetaminophen (4'-hydroxyacetanilide)	5.0 kg.
Citric acid	.60 kg.
Wild cherry imitation flavour	60.0 gm.

In preparing the candy base, the sucrose is dissolved in 5.5 liters of water, and the glucose-containing corn syrup is added and mixed well. At this point, any desired dye may be added to impart the required color. The dye must be dissolved thoroughly.

The above mixture is placed in a steam-jacketed kettle which is heated to 125° C. from which it is pumped into a storage vessel that feeds a continuous cooker. As the syrup passes through a coil in the cooker, it reaches a temperature of 125—150°C. and is then fed into a receiving kettle maintained at 28—29 inches of vacuum by means of a steam vacuum ejector for a period of about 6—7 minutes. During this period water is removed until it is reduced to about 1% or less and a suitable molten candy base is formed. The candy base then is permitted to cool slowly.

The medicament, citric acid and imitation flavor in powdered form are added to the polyethylene glycol and the mixture then heated to about 90° C. The hot liquid mixture is rapidly added to the molten candy base (the temperature of which has been reduced to about 100° C.) with adequate mixing. The total mass then is kneaded thoroughly and subsequently transferred to a spinning machine which extrudes it into lozenge forming dies. Alternatively the medicated molten candy mass can be poured onto cooling tables where it solidifies to a semi-solid mass which then may be formed into any desired shape for dispensing a unit dosage of the medicament.

EXAMPLE 2

Sucrose	35 kg.
Glucose U.S.P.	21 kg.
Polyethylene glycol (6,000 m.w.)	3 kg.
Aluminum aspirin	5 kg.
Citric acid	0.6 kg.
Orange flavor, imitation	60 gm.

EXAMPLE 3

Sucrose	35 kg.
Corn syrup 43° Baumé	21 kg.
Polyethylene glycol (6,000 m.w.)	3 kg.
Salicylamide	5 kg.
Citric acid	0.5 kg.
Citrus imitation flavor	50 gm.

EXAMPLE 4

Sucrose	35 kg.
Glucose U.S.P.	21 kg.
Polyethylene glycol (6,000 m.w.)	2.5 kg.
4-Hexylresorcinol	60 gm.
Citric acid	0.5 kg.
Phenylpropanolamine	0.12 kg.
Cyproheptadine tannate	40 gm.

EXAMPLE 5

Sucrose	35 kg.
Corn syrup 43° Baumé	21 kg.
Polyethylene glycol (6,000 m.w.)	3 kg.
Acetylsalicylic acid	3 kg.
Citric acid	0.6 kg.
Citrus type imitation flavor	60 gm.

EXAMPLE 6

Sucrose	60 kg.
Glucose U.S.P.	40 kg.
Polyethylene glycol (4,000 m.w.)	5 kg.
Acetaminophen	4 kg.
Citric acid	1.5 kg.

EXAMPLE 7

Sucrose	35 kg.
Corn syrup 43° Baumé	21 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
Acetylsalicylic acid	3 kg.
Citric acid	0.6 kg.
Orange flavor, imitation	60 gm.

EXAMPLE 8

Sucrose	85 kg.
Glucose U.S.P.	15 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
Cyproheptadine tannate	80 gm.
Citric acid	1.5 kg.
Citrus imitation flavor	0.15 kg.

EXAMPLE 9

Sucrose	65 kg.
Glucose U.S.P.	35 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
d-methorphan tannate (tannate salt of d-3-methoxy-N-methylmorphinan)	0.2 kg.
Citric acid	1.5 kg.

EXAMPLE 10

Sucrose	35 kg.
Corn syrup 43° Baumé	21 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
Phenylephrine hydrochloride	0.1 kg.
Citric acid	0.5 gm.
Citrus imitation flavor	60 gm.

EXAMPLE 11

Sucrose	65 kg.
Glucose U.S.P.	35 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
4-Hexylresorcinol	0.1 kg.
Citric acid	1.5 kg.

EXAMPLE 12

Sucrose	35 kg.
Corn syrup 43° Baumé	21 kg.
Polyethylene glycol (4,000 m.w.)	3 kg.
Phenyl propanolamine	0.1 kg.
Citric acid	0.5 kg.
Citrus imitation flavor	60 gm.

EXAMPLE 13

Sucrose	67 kg.
Glucose U.S.P.	33 kg.
Polyethylene glycol (20,000 m.w.)	5 kg.
Acetaminophen	10 kg.
Citric acid	1.5 kg.
Citrus imitation flavor	0.1 kg.

In each of the examples 2 to 13, the sucrose and glucose or corn syrup are dissolved in about 5 liters of water and heated to form a molten candy base employing the equipment and method described in Example 1 and then allowed to cool slowly to about 90—100° C.

The medicament and other ingredients are dissolved in the polyethylene glycol by the process also described in Example 1 and then added to the hot candy base and worked up into any desired form containing a unit dosage of the medicament as suggested in that example or by other methods known to those skilled in the art for extruding punching or cutting hard candy forms.

WHAT WE CLAIM IS:—

1. A process for the preparation of medicated candy lozenges comprising a medicament dispersed in a hard candy base, which comprises preparing a molten candy consisting essentially of sucrose and glucose, separately heating a mixture of the powdered medicament and a polyethylene glycol having an average molecular weight in the range 4,000—20,000 until a uniform dispersion or solution of the medicament in the polyethylene glycol is obtained, blending the said dispersion or solution with the molten candy base in an amount of from 2—16% by weight, based on the candy base, and forming the blend into lozenges.

2. A process according to Claim 1, wherein the candy base comprises from 60—85% by weight sucrose and 15—40% by weight glucose.

3. A process according to Claim 1 or 2, wherein the dispersion or solution of the medicament in polyethylene glycol blended with the candy base contains from 1—10% by weight of said medicament and from 1—6% by weight of polyethylene glycol based on the weight of the candy base.

4. A process according to Claim 3, wherein said dispersion or solution contains from 8—10% by weight of medicament based on the weight of the candy base.

5. A process according to Claim 1, substantially as hereinbefore described in any one of the Examples.

6. Medicated candy lozenges when prepared by a process claimed in any one of the preceding claims.

7. A medicated lozenge comprising a hard candy base consisting essentially of sucrose and glucose having dispersed therein from 2—16% by weight of a mixture of a medicament and a polyethylene glycol having an average molecular weight in the range 4,000—20,000.

8. A lozenge according to Claim 7, wherein the candy base comprises 60—85% by weight sucrose and 15—40% by weight glucose.

9. A lozenge according to Claim 7 or 8, wherein the lozenge contains from 1—10% by weight of said medicament and from 1—6% by weight of polyethylene glycol based on the weight of the candy base.

10. A lozenge according to Claim 9, wherein the lozenge contains from 8—10% by weight of medicament based on the weight of the candy base.

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